REMARKS

The Final Office action dated February 17, 2009 is acknowledged. Claims 1 and 3-36 are pending in the instant application. Claims 1, 3-14, 20-29 and 33-35 have been rejected and claims 15-19, 30-32 and 36 have been withdrawn. By the present Final Office Action response, claims 1, 3 and 35 have been amended and claim 7 has been cancelled. In particular, claim 1 has been amended to specify the various mucosal surfaces as well as the corresponding pH values for each type of mucosal surface, support for which may be found in the specification such as at paragraph [00020]. Claim 3 has been amended to delete gelatin and polyacrylic acid. Reconsideration is respectfully requested in light of the amendments and arguments made herein. No new matter has been added.

Rejection of claim 35 under 35 U.S.C. 112, second paragraph

The Examiner has rejected claim 35 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. In particular, the Examiner states that the Markush group language in claim 35 appears to only refer to a single item and so clarification is required. Claim 35 has been amended accordingly. Withdrawal of this rejection is requested.

Rejection of claims 1-5, 7-11, 13-15, 21, 22, 24-26 and 29 under 35 U.S.C. 102(b)

Claims 1-5, 7-11, 13-15, 21, 22, 24-26 and 29 have been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 4,572,832 (Kigasawa, et al.). The Examiner maintains the rejection as set forth in the previous Office action. In particular, the Examiner states that Kigasawa, et al. disclose every limitation recited in the

aforementioned claims, namely, soft buccal compositions which comprise a medicament to be absorbed through the oral cavity, a water-soluble protein, a polyhydric alcohol and a fatty acid ester and/or a carboxyvinyl polymer. The Examiner also believes that the reference discloses a soft buccal comprising the active ingredient pindolol which is prepared using the film forming polymer gelatin (gelatine), pH 6.5 phosphate buffer and the excipients propylene glycol, medium-chain fatty acid triglycerides, sucrose fatty acid ester, glycerin, mannitol and corn starch (col. 12, lines 43-60; Example 8). The Examiner further states that the total weight of the excipients is about 70% of the total weight of the product and that after sonication to create a dispersion, the gelatin was added and the resulting mixture kneaded and cut into plate-shaped (i.e., a film-shaped) dosage form, which took between 16 minutes and 17 minutes - 15 seconds to disintegrate. The Examiner thus concludes that Kigasawa, et al. teach a film-shaped, dried dosage form comprising an active ingredient and at least one matrix-forming polymer whose pH value is adapted to the physiological pH value of the mucosa to which the administration form is to be applied.

The Applicants respectfully disagree with the Examiner's conclusion and submit that the present invention as defined in the present claims is patentably distinct from the invention disclosed in the prior art Kigasawa, et al. reference. In particular, the presently amended claims recite that a specific pH value is required depending on the target mucosa to which the administration form is to be applied. Therefore, the Examiner's arguments on page 4, lines 13-22 of the Final Office action are no longer germane.

In this regard, it is stated in the Office action (page 4, last 4 lines – page 5, line 3) that "regardless of the exact pH of the final composition, the pH is 'approximated or

adapted to the physiological values of the mucosas to which the administration form is to be applied'." The Applicants respectfully submit that this assertion is merely speculative since without intentional adjustment of the pH (according to the present invention), it cannot be predicted or assumed that the pH of the final composition will correspond to the physiological pH of the target mucosa in each particular case. For example, the "soft buccals" of Example 8(b) of Kigasawa, et al. were adjusted to pH 6.5 (column 12), and the oral mucosa of albino rabbits was used as a test system (column 16). Although "Test Example 2" described in column 16 relates to the soft buccals of Example 8(a) rather than Example 8(b), it is readily clear that the pH to which the soft buccals of Example 8(b) were adjusted (i.e., pH 6.5) is not suitable for administration to a herbivore (e.g., rabbit) mucosa based on the pH values indicated for herbivoral mucosa in present claim 1.

Regarding Example 8(a) of Kigasawa, et al., no pH adjustment step is taught in the description of the manufacturing method (column 12). Therefore, the Applicants submit that it remains speculative whether the pH of the thus-obtained soft buccals, when administered to the target mucosa of albino rabbits (column 16), was in the pH range of 8-9 as would be required in accordance with present claim 1 for herbivoral mucosa.

In addition, Kigasawa, et al. fails to teach that the pH of the soft buccals described therein should be adjusted differently, depending on whether the soft buccals are designed to be administered to a human oral mucosa or a rabbit (herbivoral) oral mucosa. In contrast thereto, present claim 1 recites that the pH is adjusted to 8-9 when the mucosa is a herbivoral mucosa and to 5.5 to 6.5 when the mucosa is a human oral mucosa.

With respect to dependent claim 3, the Applicants further submit that Example

8(b) of Kigasawa, et al., which is the passage referring to a specific pH value, concerns a composition based on gelatin as the only matrix polymer. Gelatin is excluded from the list of matrix polymers recited in present claim 3.

In conclusion, it is submitted that Kigasawa, et al. fail to teach each and every limitation of the present claims, and therefore fail to anticipate the present invention as set forth in the present claims. Withdrawal of this rejection is respectfully requested.

Rejection of claims 1-14, 20-29 and 33-35 under 35 U.S.C. 103(a)

Claims 1, 3-11, 13-14, 20-29 and 33-35 have been rejected as being unpatentable over Kigasawa, et al. for the reasons set forth in the previous Office action. In particular, the Examiner states that Kigasawa, et al. disclose soft buccal compositions which comprise a medicament to be absorbed through the oral cavity, a water-soluble protein, a polyhydric alcohol and a fatty acid ester and/or a carboxyvinyl polymer. The Examiner also states that forms include sheets, bands and disks. The Examiner further states that the reference discloses a soft buccal comprising the active ingredient pindolol which is prepared using the film forming polymer gelatin (gelatine), pH 6.5 phosphate buffer and the excipients propylene glycol, medium-chain fatty acid triglycerides, sucrose fatty acid ester, glycerin, mannitol and corn starch. The Examiner still further states that the total weight of the excipients is about 70% of the total weight of the product and that after sonication to create a dispersion, the gelatin was added and the resulting mixture kneaded and cut into plate-shaped (i.e., a film-shaped) dosage form, which took between 16 minutes and 17 minutes, 15 seconds to disintegrate. The Examiner thus concludes that Kigasawa, et al. teach a film-shaped, dried dosage form comprising an active ingredient

and at least one matrix-forming polymer whose pH value is adapted to the physiological pH value of the mucosa to which the administration form is to be applied.

The Examiner states that Kigasawa, et al. fail to explicitly prepare administration forms which contain aroma substances or cellulose derivatives or an administration form which disintegrates in less than 10 minutes. However, the Examiner argues that Kigasawa, et al. does disclose that additives can be added in addition to the required ingredients, including flavorings (i.e., aroma substances), such as menthol, lemon oil and citrus flavors, as well as other excipients, disintegrating adjusting agents, emulsifiers, dispersants, binders and thickeners. Additionally, the Examiner states that the reference discloses that for the required polyhydric alcohol component, ingredients can be ethylene glycol, propylene glycol or polyethylene glycol, and that included in the category of polyhydric alcohols are cellulose and cellulose derivatives such as methyl cellulose, ethyl cellulose, hydroxymethyl cellulose, hydroxyethyl cellulose and carboxymethyl cellulose.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a dosage form with an aroma ingredient, taught by Kigasawa, et al., as an ingredient to impart a flavor/aroma to the medicament and to use a cellulose derivative such as ethyl cellulose for the required polyhydric alcohol component of the film administration. The Examiner also states that the amount of an aroma ingredient in a composition is clearly a result effective parameter that one skilled in the art would routinely optimize, and the aroma/flavor chosen and the strength of the aroma/flavor desired or required in the composition, such as to mask the taste of a bitter active ingredient, would determine the amount of the ingredient present in the composition. The Examiner further states that one skilled in the art would adjust the

composition of the tablet in order to provide a fast disintegration of the dosage form to minimize the possibility for swallowing the dosage form and losing the benefits of the buccal administration form.

Regarding claims 33 and 34, the Examiner states that Kigasawa, et al. teach that pharmaceutically active ingredients in the salt form are suitable for incorporation into the soft buccal form and that the salts triperizone hydrochloride, dantrolene sodium, cyclobenzaprine hydrochloride and ipratroprium bromide are exemplified. The Examiner further states that menthol (which reads on aroma substance) can be included in the soft buccal dosage form. Therefore, the Examiner concludes that a dosage with only menthol in the base mass will meet the limitation of claim 35 in which the active substance present in the film-shaped administration form is an aroma substance.

Claims 1, 3-14, 20-29 and 33-35 have been rejected as being unpatentable over Kigasawa, et al., as applied to claims 1, 3-11, 13-15, 20-29 and 33-35 above, and further in view of U.S. Patent No. 5,900,247 (Rault, et al.) for the reasons set forth in the previous Office action. In particular, the Examiner states that Kigasawa, et al. disclose soft buccal administration forms of active ingredients that can be formulated as disks or wafers, as discussed above. However, the Examiner states that Kigasawa, et al. fail to disclose a multilayer dosage form.

The Examiner refers to Rault, et al. and states that the reference discloses a bioadhesive pharmaceutical composition to locally release active ingredients through various mucosal membranes, and that the bioadhesive composition comprises a vinyl acetate/polyvinylpyrrolidinone copolymer, at least one active ingredient, optionally a cellulose or cellulose derivative such as ethyl cellulose or hydroxypropylmethyl cellulose

and excipients such as plasticizers, flavoring agents or sweeteners. The Examiner further states that after spreading of the bioadhesive mixture onto a biodegradable or non-biodegradable protective film or substrate, the assembly is dried and the protective film is chosen for its adhesive or bioadhesive properties and is peelable. According to the Examiner, this process results in the production of a multilayered administration form and that in Example 4 of the reference, a composition is prepared which contains approximately 3% by dry weight of flavoring agents.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a buccal administration form as taught by Kigasawa, et al. and to place this material on a protective film as taught by Rault, et al., resulting in a multilayered administration form. The Examiner also concludes that Rault, et al. provide additional guidance to one skilled in the art as to the amount of flavoring ingredients, which can include aroma substances, that can be added to such compositions.

It is respectfully submitted that to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The Applicants respectfully submit that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at the present invention. Additionally, even if one skilled in the art were to consider the teachings of the cited prior art alone or in combination, each and every limitation of the present invention would not be disclosed, nor would there be a reasonable expectation of success if the aforementioned references

were to be considered.

The Applicants still respectfully disagree with the Examiner's position for at least the numerous deficiencies of Kigasawa, et al. set forth above. In particular, the Examiner's conclusions have been based on the assumption that Kigasawa, et al. teach film-shaped dosage forms whose pH value is adapted to the physiological pH value of the mucosa to which the administration form is to be applied. As discussed above, this rationale does not apply to the present claims since Kigasawa, et al. fail to teach pH adjustment in the specified ranges, depending on whether the administration form is to be applied to the oral mucosa of a herbivore, to the human oral mucosa, to the human nasal mucosa or to the human vaginal mucosa. Therefore, it is submitted that the Examiner's rationale for supporting an obviousness rejection as set forth in the previous Office action is no longer germane.

Regarding claims 33 and 34, the Examiner states that Kigasawa, et al. teach active ingredients in the salt form that would be suitable for incorporation into the soft buccal form. However, as discussed above, Kigasawa, et al. teach pH adjustment only in connection with Example 8(b) and therefore this teaching cannot be interpreted as being applicable to the remaining examples as well. Kigasawa, et al. also fail to teach a general pH adjustment. Example 8(b), however, relates to a pharmaceutical active substance (pindolol) which was not incorporated in salt form, but rather as a free base. In turn, Kigasawa, et al. fail to teach pH adjustment in the case where active substances are added in salt form.

As set forth in the Office action, the Examiner refers to Rault, et al. simply for teaching a multilayered administration form as set forth in dependent claim 12. Clearly,

Rault, et al. fail to make up for any of the numerous aforementioned deficiencies of Kigasawa, et al. and therefore the combination with Kigasawa, et al. would fail to teach or disclose each and every limitation of the presently claimed invention – in particular with each and every limitation of present claim 1. Therefore, the Applicants respectfully request that this obviousness rejection be withdrawn.

Conclusion

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments, amendments to the claims and deficiencies of the prior art references, the Applicants strongly urge that the obviousness-type rejection and anticipation rejections be withdrawn. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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